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6,156,354

DOCUMENT-IDENTIFIER: US ~~6503545~~ B1
TITLE: Hyper-absorption of vitamin E combined with milk protein

Brief Summary Text (2):
This invention relates to milk-based food products, and in particular to the microdispersal of vitamin E in milks (milkfat-based milk, skim milk, vegetable oil-filled milk, and blends thereof) at a level providing at least 31 IU (International Units) per serving. The invention also relates to a substantially lactose-free and milkfat-free composition for oral administration to a human or other mammal, including a microdispersed mixture of at least one mammalian milk protein or fragment thereof, and at least one fat-soluble micronutrient or pharmaceutical agent, where the weight ratio of said mammalian milk protein to said fat-soluble micronutrient or pharmaceutical agent is between 1:1 and 1000:1.

Brief Summary Text (7):
In a separate area of nutritional biochemistry, Perlman et al. in U.S. Pat. No. 5,514,407 combined vegetable oils rich in polyunsaturated fatty acids, with cholesterol-reduced animal fats rich in saturated fatty acids to produce oxidation-resistant fat blends containing 1-10 parts by weight of the animal fat to 1 part of vegetable oil. These blends showed favorable nutritional characteristics in mammals, including a decreased total serum cholesterol level, and a decreased LDL/HDL cholesterol ratio in humans. In Sundram et al., U.S. Pat. No. 5,578,334 and Sundram et al., U.S. Pat. No. 5,843,497 (which are hereby incorporated by reference in their entireties including drawings), certain vegetable oils such as soybean oil, rich in polyunsaturated fatty acids, were combined with palm oil, rich in saturated fatty acids, to produce dietary fat blends containing approximately equal proportions of saturated and polyunsaturated fatty acids (hereinafter termed "balanced fats"). Compared to diets in which one class of fatty acids predominates (polyunsaturated, monounsaturated or saturated), if such balanced fats are consumed as the principal dietary fat (at approximately 30% of dietary calories supplied as fat), the ratio of plasma LDL to HDL cholesterol is beneficially reduced. At the same time, HDL levels are beneficially sustained or increased.

Brief Summary Text (9):
Concerning the uptake of vitamin E in mammals, several synthetic additives known for dispersing or dissolving fats and other lipophilic substances have been combined with vitamin E and reported to increase absorption of vitamin E. Greene et al., U.S. Pat. No. 5,179,122 describe a composition including vitamin E, an edible surfactant and an inert carrier for increasing the bioavailability of vitamin E. Julianto et al. (Int J Pharmaceutics, 200 (1): 53-57, 2000) describe a self-emulsifying formulation consisting of vitamin E dissolved in palm oil, plus a combination of the synthetic non-ionic surfactants, Tween 80 and Span 80 (esters and ester-ethers of fatty acids). DeMichele et al., U.S. Pat. No. 6,013,665 describe a method for enhancing absorption of a lipophilic compound such as an oil-soluble vitamin by administering structured triglycerides together with the lipophilic compound. In the Background section of U.S. Pat. No. 6,013,665, the authors also include a substantial review of the prior art describing "absorption promoters" for lipophilic compounds such as vitamin E. These include combinations of vitamin E with medium chain and structured triglycerides for enteral and parenteral preparations, and vitamin E dispersed with lecithin and unsaturated fatty acids for dietary supplements. The patent also describes research in which the dietary inclusion of unsaturated fatty acids actually depresses vitamin E absorption. Likewise, ingestion of dietary fiber, e.g.,pectin, guar or cellulose, together with vitamin E and carotenoids has been reported to reduce the bioavailability of these antioxidants (Hoffmann et al., Eur J Nutr, 38(6): 278-285, 1999). In summary, research on food

rather than ingesting 2-3 times the amount in capsule form. In preferred embodiments, the milk product provides a 2-3-fold increase in bioavailability over the capsule form of vitamin E such that the increase in bioavailability outweighs the losses in vitamin E activity during processing and storage of the milk product. That is the reduction in the amount of vitamin E need to achieve a particular increase in vitamin E/cholesterol ratio is greater than the processing loss (as either amount or percentage). Preferably the ratio of beneficial reduction to undesirable loss is at least 1.25, 1.5, or 1.75.

Brief Summary Text (59):
In preferred embodiments of this and other aspects of this invention, the milk product is selected from the group of products including whole milk, reduced-fat milk, low-fat milk, skim milk, vegetable oil-filled milk, blended vegetable oil and milkfat-filled milk, lactose-reduced milk (milk in which some or all of the disaccharide milk sugar, lactose, has been enzymatically converted to the monosaccharides, glucose and galactose), butter milk, flavored milk, dairy-containing beverages, yoghurt, cream, sour cream, ice cream, cream cheese, cottage cheese, hard and soft cheeses (e.g., cheddar, Swiss and mozzarella), processed cheese (e.g., American cheese) butter and butter-containing spreads, puddings, eggnog, powdered and reconstituted milk, concentrated milk, condensed milk, milk-based infant formula, and the like.

Brief Summary Text (64):
In preferred embodiments the chemical form of the vitamin E in the milk product is selected from the group consisting of all-rac-.alpha.-tocopherol acetate, all-rac-.alpha.-tocopherol, RRR-.alpha.-tocopherol acetate, RRR-.alpha.-tocopherol and combinations thereof. The physical form of the vitamin E in the milk product is selected from the group consisting of water-dispersible and oil-dispersible preparations.

Brief Summary Text (66):
In preferred embodiments, the milk product includes a milkfat-containing cream portion and an oil-dispersible preparation of vitamin E which is microdispersed throughout the cream portion and throughout the product. Alternatively, the milk product is a filled milk product which includes a polyunsaturated, and/or monounsaturated vegetable oil-containing cream portion which may also include milkfat, and an oil-dispersible preparation of vitamin E which is microdispersed throughout the cream portion and throughout the product. Alternatively, the milk product is fat-free, and includes a water-dispersible preparation of vitamin E which is microdispersed throughout the product.

Brief Summary Text (68):
As described above, microdispersal of at least 50 IU vitamin E per serving in a milk product advantageously provides at least 100 IU in 1 to 2 servings. Recognition in the present invention that milk is a particularly effective delivery vehicle for vitamin E suggests that a level of vitamin E elevated above 30 IU per serving of milk is helpful, as it allows a quantity of vitamin E sufficient to provide substantial health benefits to be provided in fewer servings of a milk product than with previous milk products. Thus, in a related aspect, the invention features a milk product which includes at least 31 IU of vitamin E per serving of the product and preferably at least 40 IU per serving (or 50, 60, 80, 100, 200, 400 IU per serving). The vitamin E is microdispersed throughout the milk product. Daily ingestion of at least 50 up to 400 IU daily of the milk product causes the fasting vitamin E/cholesterol ratio to be elevated over the basal fasting vitamin E/cholesterol ratio to at least a two-fold greater extent than that elevation achieved by daily ingestion of the same quantity and chemical species of vitamin E provided in the form of a pharmacological capsule or pill. By contrast, with lower levels of vitamin E ingestion, such as 30 IU per day, only small, if any, differences exist between the absorption from capsules compared to absorption from milk.

Brief Summary Text (75):
In still another aspect, the invention features a method for beneficially fortifying a milk product with a defined quantity and chemical form of vitamin E. The milk product includes at least 31 IU of microdispersed vitamin E, preferably at least 40

with previous milk products. Thus, in a related aspect, the invention features a milk product which includes at least 31 IU of vitamin E per serving of the product and preferably at least 40 IU per serving (or 50, 60, 80, 100, 200, 400 IU per serving). The vitamin E is microdispersed throughout the milk product. Daily ingestion of at least 50 up to 400 IU daily of the milk product causes the fasting vitamin E/cholesterol ratio to be elevated over the basal fasting vitamin E/cholesterol ratio to at least a two-fold greater extent than that elevation achieved by daily ingestion of the same quantity and chemical species of vitamin E provided in the form of a pharmacological capsule or pill. By contrast, with lower levels of vitamin E ingestion, such as 30 IU per day, only small, if any, differences exist between the absorption from capsules compared to absorption from milk.

Brief Summary Text (50):
In still another aspect, the invention features a method for beneficially fortifying a milk product with a defined quantity and chemical form of vitamin E. The milk product includes at least 31 IU of microdispersed vitamin E, preferably at least 40 or 50 IU, more preferably at least 60, 80, 100, 200, 400, or more IU per serving of the product. Daily ingestion of an amount of the milk product containing at least 100 IU causes an increase in the fasting plasma vitamin E/cholesterol ratio which is at least two-fold greater than that increase caused by daily ingestion of the same defined quantity and chemical form of vitamin E provided in the form of a pharmacological capsule or pill in the forms currently prepared. The method includes microdispersing the defined quantity and chemical form of vitamin E throughout the milk product.

Brief Summary Text (53):
The term "milk product" includes milk and/or cream-based products in whatever form, including, for example, liquid milks [including fat-free skim milk, whole milk, low-fat milk, reduced fat milk, butter milk, lactose-reduced milk and filled milks in which the milkfat portion of the milk is partially or completely replaced by a monounsaturated vegetable oil (e.g., canola oil) or a polyunsaturated vegetable oil (e.g., soybean oil)], as well as yoghurts, creams, sour cream, ice cream, cream cheese, cottage cheese, hard and soft cheeses, processed cheese, e.g., American cheese, buttermilk, egg nog, powdered and reconstituted milk, concentrated milk, condensed milk, and milk-based infant formula.

Brief Summary Text (56):
The term "microdispersed" or "microdispersing" with regard to fat-soluble vitamin E (tocopherol or tocopherol acetate) refers to a process for blending or dissolving the vitamin E into the cream (milkfat-containing) portion of regular milk, or into the vegetable oil (e.g., soybean oil) component or blended vegetable oil and milkfat component of filled milks, and then pasteurizing and homogenizing the milk to reduce the diameter of most (>90%) of the fat particles to less than 2 microns. Thus, microdispersal ultimately distributes vitamin E into the small, stable microscopic fat particles which are present in homogenized milk. In the case of skim milk and other fat-free foods, the vitamin E is generally added as a pre-mixed, water-dispersible blend. For example, Roche Vitamins, Inc. (Paramus, N.J.) and Watson Foods Co., Inc (West Haven, Conn.) produce all-rac-.alpha.-tocopherol acetate in cold water-dispersible powder forms containing approximately 50% by weight vitamin E and 50% by weight of an emulsifier/dispersant system. In the Roche product, the dispersant consists primarily of dextrin and gelatin in a 3:2 weight ratio, while in the Watson product (used in the present clinical study), the dispersant is modified food starch. These dispersant systems allow the vitamin E to remain stably suspended, in a fine colloidal dispersion, within skim milk. To assure microdispersal of vitamin E throughout skim milk, the milk was pasteurized and homogenized, using methods well known in the art, after the water-dispersible vitamin E had been added to the milk. It is unknown whether microdispersal of vitamin E in skim milk is aided by natural components of the skim milk including the milk proteins, casein and lactalbumin, for example. The term "microdispersal" with regard to vitamin E dispersal in a milk product, also has a functional definition. If the vitamin E has been sufficiently well mixed, blended, emulsified, homogenized, or otherwise dispersed into a milk product, it has been "microdispersed" if the bioavailability of a dose of vitamin E, when tested in humans is at least two times (e.g., 2-3 times) greater (i.e., the increase over basal fasting vitamin